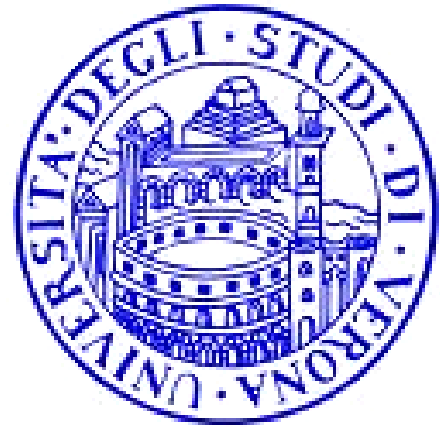


# Covid 19 :

## *the role of the pediatrician this fall and winter*



- ✓ Introduction: the second wave has arrived !
- ✓ Covid 19 no/yes by symptoms
- ✓ The case of the allergic child
- ✓ Covid 19 testing
- ✓ How to prepare the immune system
- ✓ The importance of nasal washing
- ✓ Waiting for a specific vaccine, do the others!
- ✓ Summary & Conclusions

Attilio Boner  
University of  
Verona, Italy

[attilio.boner@univr.it](mailto:attilio.boner@univr.it)

# Prevalence of SARS-CoV-2 Infection in Children Without Symptoms of Coronavirus Disease 2019.

*Sola AM, JAMA Pediatr. 2020 Aug 25*

✓ prevalence of SARS-CoV-2 infection in children who are asymptomatic (age range, 0-18 years) reported by pediatric otolaryngologists

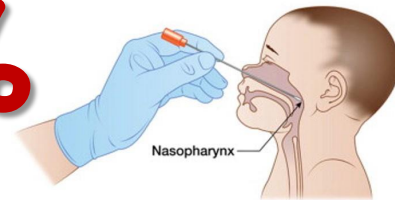
✓ Reverse transcription-polymerase chain reaction tests for SARS-CoV-2 RNA performed before surgery, clinic visits, or hospital admissions.

✓ mean weekly incidence of COVID-19 for the entire population of the combined statistical area (CSA)

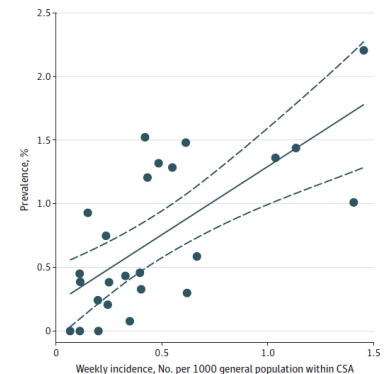
➤ of 33 041 asymptomatic children tested 250 resulted positive for SARS-CoV-2 with



a prevalence of **0.65%**



➤ Asymptomatic pediatric prevalence was significantly associated with incidence of COVID-19 in the general population



**Prevalence** refers to proportion of persons who have a condition at or during a particular time period,

**Incidence** refers to the proportion or rate of persons who develop a condition during a particular time period.

# Prevalence of SARS-CoV-2 Infection in Children Without Symptoms of Coronavirus Disease 2019.

*Sola AM, JAMA Pediatr. 2020 Aug 25*

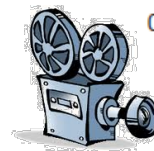
✓ prevalence of SARS-CoV-2 infection in children who are asymptomatic (age range, 0-18 years) reported by pediatric otolaryngologists



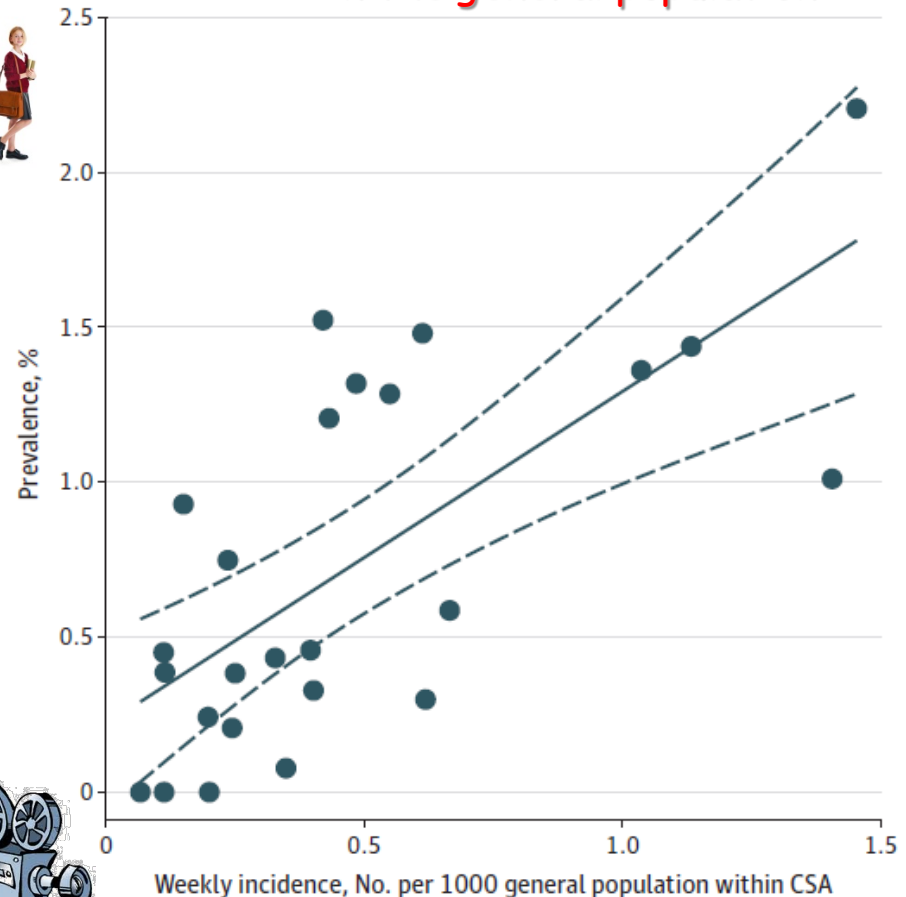
✓ Reverse transcription-polymerase chain reaction tests for SARS-CoV-2 RNA performed before surgery, clinic visits, or hospital admissions.



✓ mean weekly incidence of COVID-19 for the entire population of the combined statistical area (CSA)

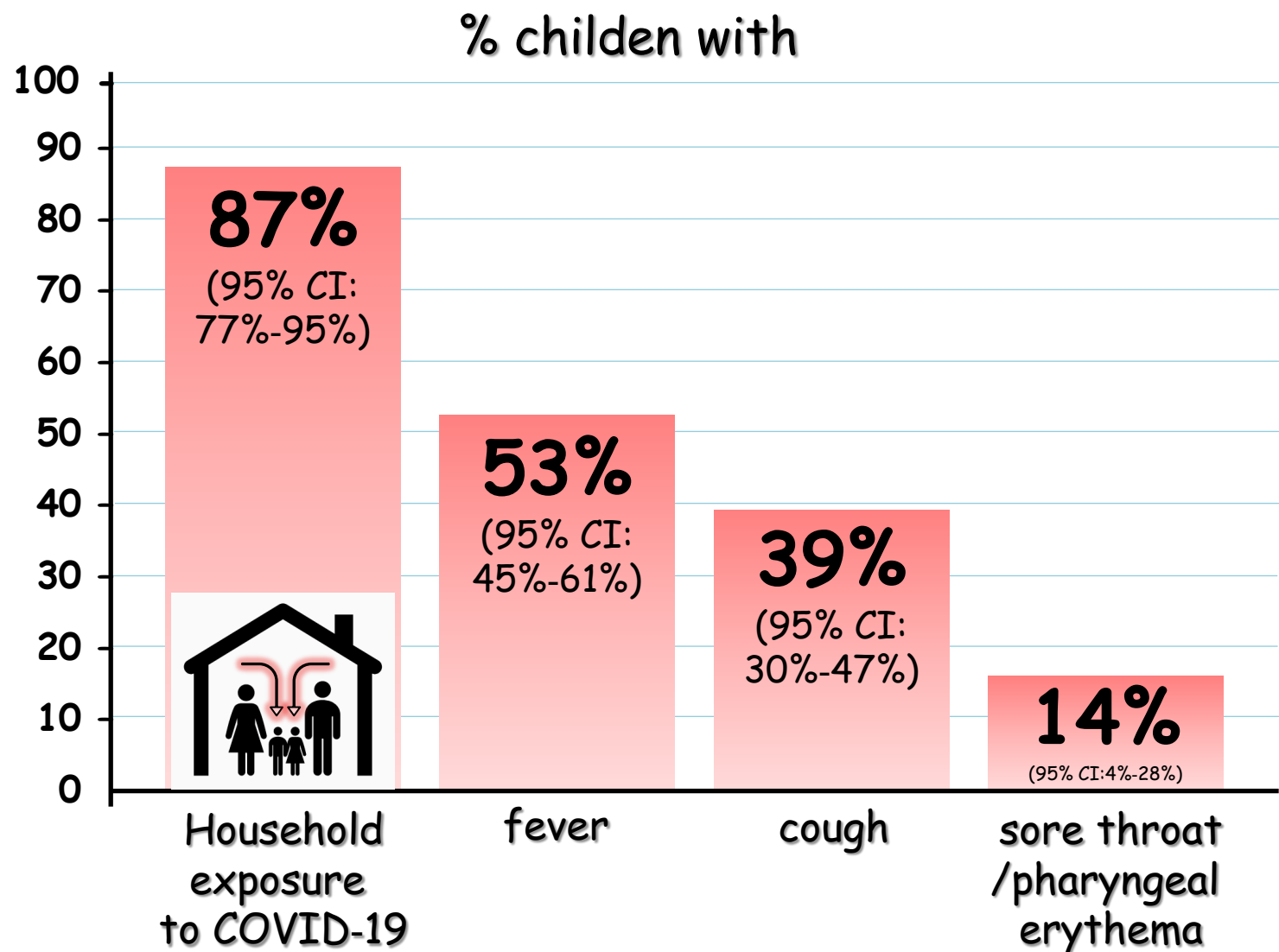


There is a strong association between prevalence of asymptomatic SARS-CoV-2 in children and contemporaneous weekly incidence of COVID-19 in the general population



# What we know so far about Coronavirus Disease 2019 in children: A meta-analysis of 551 laboratory-confirmed cases. Zhang L, *Pediatr Pulmonol.* 2020;55(8):2115-2127.

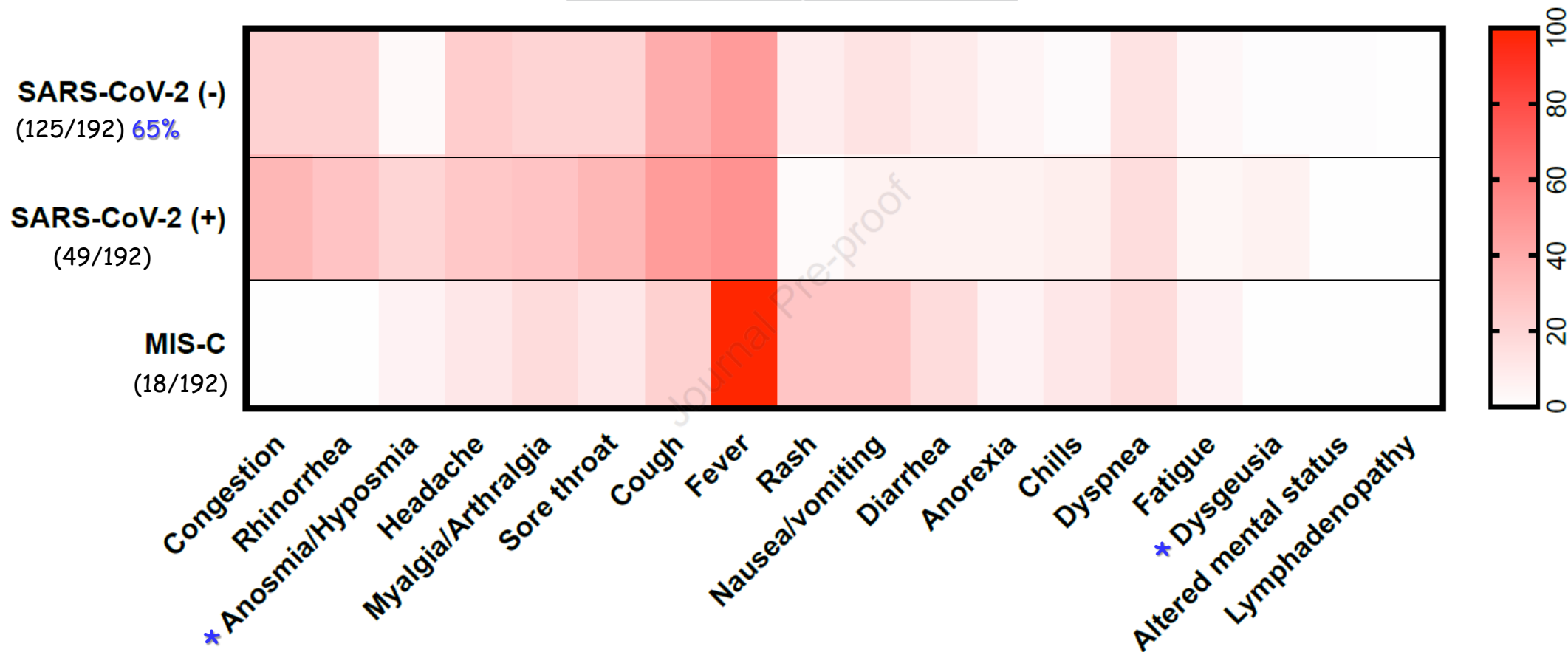
✓ 46 articles reporting 551 cases of COVID-19 in children (aged 1 day-17.5 years) with laboratory-confirmed COVID-19



# Pediatric SARS-CoV-2: Clinical Presentation, Infectivity, and Immune Responses

*Yonker LM, J Pediatr. 2020;S0022-3476(20)31023-4.*

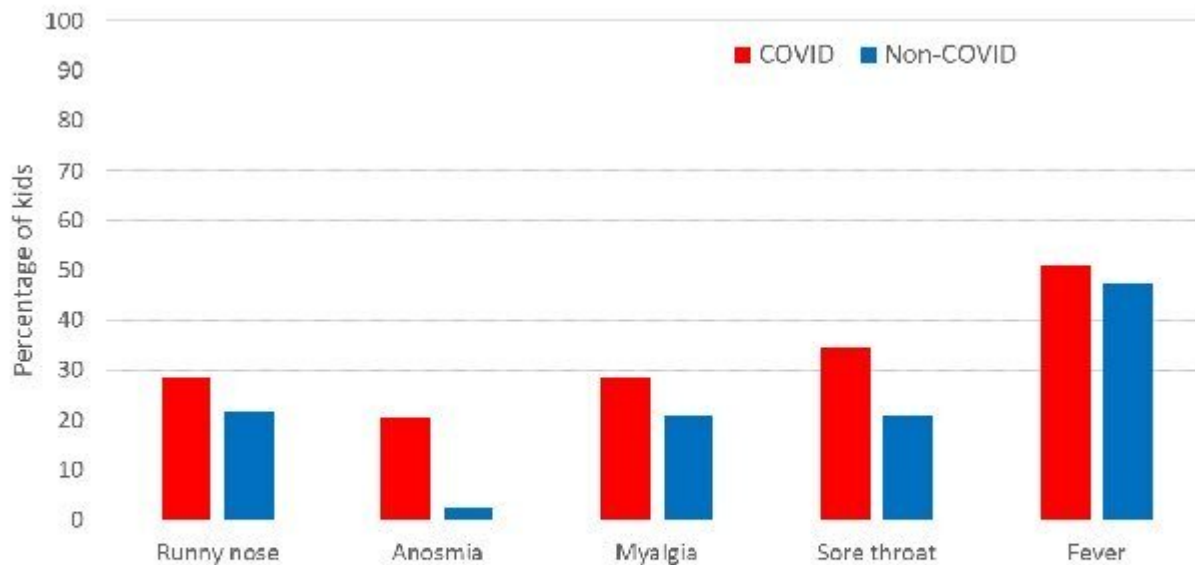
symptoms of SARS-CoV-2 infection, if present, were non-specific.



# Pediatric SARS-CoV-2: Clinical Presentation

*Yonker LM, J Pediatr. 2020;S0022-3476(20)31023-4.*

## % children with signs & symptoms



- It was pretty hard to distinguish the acute COVID-infected kids from kids with other infections on the basis of symptoms alone.

- Anosmia was more common in COVID, but only 20% of the COVID-positive kids had that symptom.

- Fever was present in about half of kids regardless.

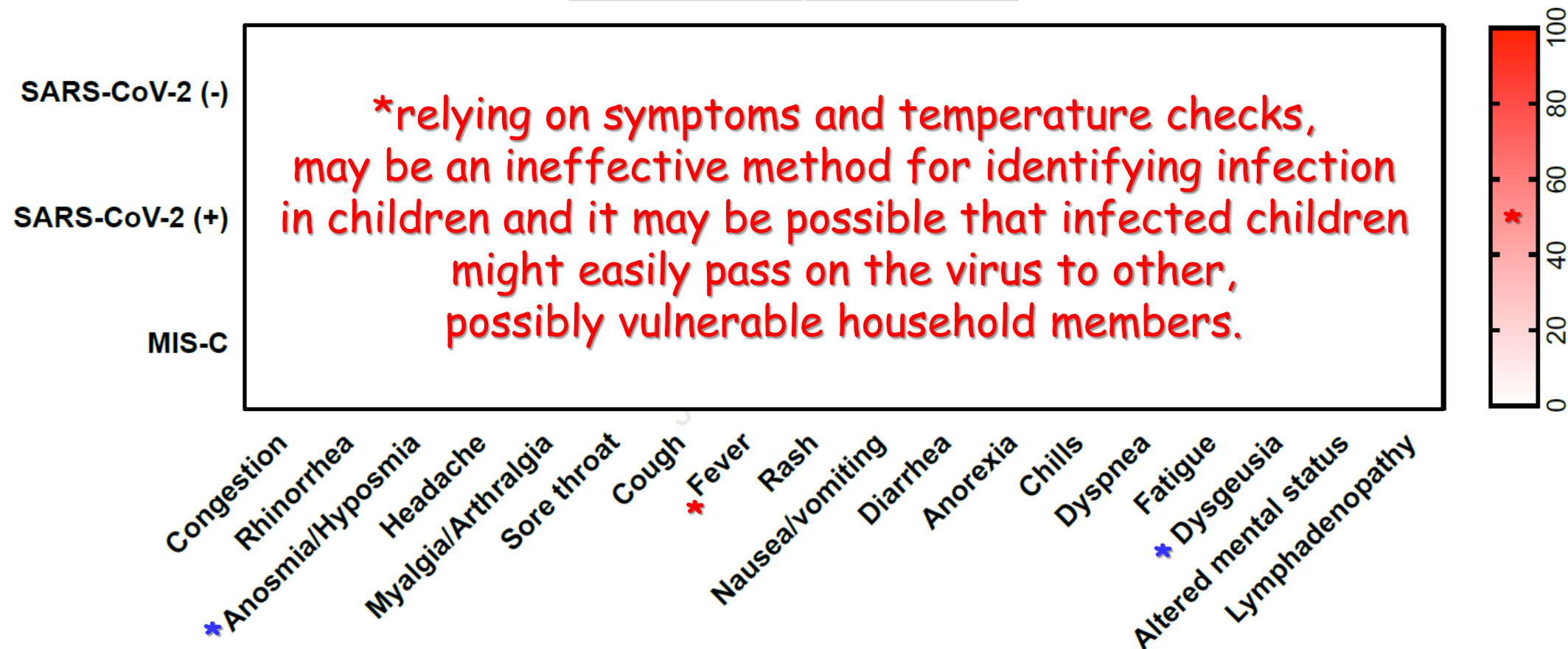


# Pediatric SARS-CoV-2: Clinical Presentation

Yonker LM, J Pediatr. 2020;S0022-3476(20)31023-4.

✓ 192 children (mean age 10.2 +/- 7 years)

symptoms of SARS-CoV-2 infection, if present, were non-specific.



\* Around 50% of children with Covid 19 have fever  $\geq 37.5^{\circ}C$  but this is true also in all respiratory infections

# Comparison of Clinical Features of COVID-19 vs Seasonal Influenza A and B in US Children.

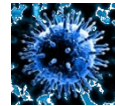
*Song X, JAMA Netw Open. 2020 Sep 1;3(9):e2020495.*

% patients hospitalized with:

COVID-19



seasonal  
influenza



reporting

•fever

76%

55%

$P = 0.005$

•diarrhea  
or vomiting

26%

12%

$P = 0.01$

•headache

11%

3%

$P = 0.01$

•body ache  
or myalgia

22%

7%

$P = 0.001$

•chest pain

11%

3%

$P = 0.01$

✓retrospective cohort study

✓315 children diagnosed with laboratory-confirmed COVID-19 between March 25 and May 15, 2020,

✓1402 children diagnosed with seasonal influenza between October 1, 2019, and June 6, 2020, at Children's National Hospital in the District of Columbia.



# Comparison of Clinical Features of COVID-19 vs Seasonal Influenza A and B in US Children.

Song X, JAMA Netw Open. 2020 Sep 1;3(9):e2020495.

Differences between patients hospitalized with COVID-19 vs influenza who reported cough (48% vs 31%  $P = 0.05$ ) and shortness of breath (30% vs 20%,  $P = 0.13$ ) were not statistically significant.

reporting

•fever

•diarrhea  
or vomiting

•headache

•body ache  
or myalgia

•chest pain

% patients hospitalized with:

COVID-19



76%

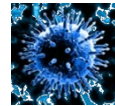
26%

11%

22%

11%

seasonal  
influenza



55%

12%

3%

7%

3%

$P = 0.005$

$P = 0.01$

$P = 0.01$

$P = 0.001$

$P = 0.01$

More extra-respiratory S&S

# COVID-19 in children and adolescents in Europe: a multinational, multicentre cohort study.

*Götzinger F, Lancet Child Adolesc Health. 2020;4(9):653-661.*

## CORONAVIRUS RISK FACTORS



## Significant risk factors for requiring ICU admission were:



- < 1 month of age (**OR = 5.06**, 95% CI 1.72-14.87;  $p=0.0035$ ),
- male sex (**OR = 2.12**, 1.06-4.21;  $p=0.033$ ),
- pre-existing medical conditions (**OR = 3.27**, 1.67-6.42;  $p=0.0015$ ),
- presence of lower respiratory tract infection signs or symptoms at presentation (**OR = 10.46**, 5.16-21.23;  $p<0.0001$ ).

✓ 82 participating health-care institutions across 25 European countries

✓ 582 individuals with PCR-confirmed SARS-CoV-2 infection (median age 5.0 years)

# Duration of symptoms of respiratory tract infections in children: systematic review.

*Thompson M, BMJ. 2013 Dec 11;347:f7027.*



✓ Of 22,182 identified references, 23 trials and 25 observational studies met inclusion criteria

In 90% of children symptoms resolved for:

• earache by 7 to 8 days,



• sore throat between 2 and 7 days,



• croup by 2 days,



• bronchiolitis by 21 days,



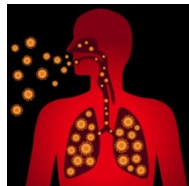
• acute cough by 25 days,



• common cold by 15 days, and

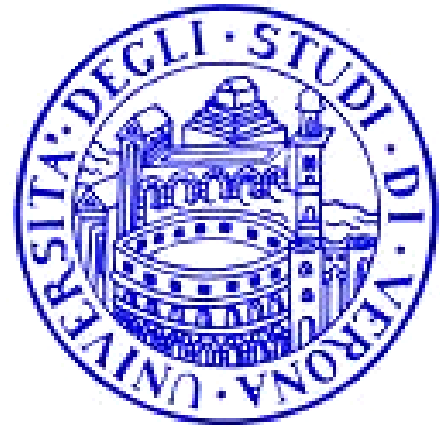


• non-specific respiratory tract infections symptoms by 16 days.



# Covid 19 :

## *the role of the pediatrician this fall and winter*



- ✓ Introduction: the second wave has arrived !
- ✓ Covid 19 no/yes by symptoms
- ✓ **The case of the allergic child**
- ✓ Covid 19 testing
- ✓ How to prepare the immune system
- ✓ The importance of nasal washing
- ✓ Waiting for a specific vaccine, do the others!
- ✓ Summary & Conclusions

*Attilio Boner*  
*University of*  
*Verona, Italy*

*attilio.boner@univr.it*

# Similarities and differences between seasonal allergic rhinitis and COVID- 19 symptoms

## PHENOTYPE

### Seasonal Allergic Rhinitis



### COVID 19

Itching  
Conjunctivitis

Nasal blockage  
Rhinorrhoea  
Sneezing

Fever  
Malaise  
Myalgia  
Anosmia  
Dry cough  
Diarrhoea







Symptoms	Coronavirus <sup>+</sup> (COVID-19) Symptoms range from mild to severe	Cold Gradual onset of symptoms	Flu Abrupt onset of symptoms	Seasonal Allergies Abrupt onset of symptoms	Asthma Gradual or abrupt onset of symptoms
 Length of symptoms	7-25 days	Less than 14 days	7-14 days	Several weeks	Can start quickly or last for hours or longer*
 Cough	Common (usually dry)	Common (mild)	Common (usually dry)	Rare (usually dry unless it triggers asthma)	Common (can be dry or wet/productive)



\*If your quick-relief medicine is not helping your asthma symptoms, or if you are in the Red Zone on your Asthma Action Plan, call your health care provider or seek medical attention immediately.





Sources: Asthma and Allergy Foundation of America, World Health Organization, Centers for Disease Control and Prevention.  
edited 7/15/20 • [aafa.org/covid19](https://aafa.org/covid19)



Symptoms	Coronavirus <sup>†</sup> (COVID-19) Symptoms range from mild to severe	Cold Gradual onset of symptoms	Flu Abrupt onset of symptoms	Seasonal Allergies Abrupt onset of symptoms	<sup>≈10% children</sup> Asthma Gradual or abrupt onset of symptoms
 Wheezing	No !	No**	No**	No**	Common
 Shortness of breath	Sometimes	No**	No**	No**	Common
 Chest tightness/ pain	Sometimes	No**	No**	No**	Common
 Rapid breathing	Sometimes	No**	No**	No**	Common





\*\*Allergies, colds and flus can all trigger asthma which can lead to shortness of breath, chest tightness/pain and rapid breathing. COVID-19 is the only one associated with shortness of breath on its own.

Sources: Asthma and Allergy Foundation of America, World Health Organization, Centers for Disease Control and Prevention.  
edited 7/15/20 • [aafa.org/covid19](https://aafa.org/covid19)

Symptoms	Coronavirus <sup>†</sup> (COVID-19) Symptoms range from mild to severe	Cold Gradual onset of symptoms	Flu Abrupt onset of symptoms	Seasonal Allergies Abrupt onset of symptoms	Asthma Gradual or abrupt onset of symptoms
 Sneezing	No?  and No itching !	Common	No	Common with itching	No***
 Runny or stuffy nose	Rare !	Common	Sometimes	Common with itching	No***
 Sore throat	Sometimes	Common	Sometimes	Sometimes (usually mild) with itching	No***

\*\*\*If you have allergic asthma, you may have symptoms of both asthma and allergies at the same time.




Sources: Asthma and Allergy Foundation of America, World Health Organization, Centers for Disease Control and Prevention.  
edited 7/15/20 • [aafa.org/covid19](https://aafa.org/covid19)

Symptoms	Coronavirus <sup>†</sup> (COVID-19) Symptoms range from mild to severe	Cold Gradual onset of symptoms	Flu Abrupt onset of symptoms	Seasonal Allergies Abrupt onset of symptoms	Asthma Gradual or abrupt onset of symptoms
 Sneezing	No?  and No itching !	Common	No	Common with itching	No ***
 Runny or stuffy nose	Rare !	Common	Sometimes	Common with itching	No ***
 Sore throat	Sometimes	Common	Sometimes	Sometimes (usually mild) with itching	No ***





\*\*\* If you have allergic asthma, you may have symptoms of both asthma and allergies at the same time.

Sources: Asthma and Allergy Foundation of America, World Health Organization, Centers for Disease Control and Prevention.  
edited 7/15/20 • [aafa.org/covid19](https://aafa.org/covid19)

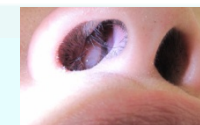


Symptoms	Coronavirus <sup>†</sup> (COVID-19) Symptoms range from mild to severe	Cold Gradual onset of symptoms	Flu Abrupt onset of symptoms	Seasonal Allergies Abrupt onset of symptoms	Asthma Gradual or abrupt onset of symptoms
 Fever	Common	Short fever period	Common	No	No
 Feeling tired and weak	Sometimes ?	Sometimes	Common	Sometimes	Sometimes
 Headaches	Sometimes ?	Rare	Common	Sometimes (related to sinus pain)	Rare

Sources: Asthma and Allergy Foundation of America, World Health Organization, Centers for Disease Control and Prevention.  
edited 7/15/20 • [aafa.org/covid19](https://aafa.org/covid19)

Symptoms	Coronavirus <sup>†</sup> (COVID-19) Symptoms range from mild to severe	Cold Gradual onset of symptoms	Flu Abrupt onset of symptoms	Seasonal Allergies Abrupt onset of symptoms	Asthma Gradual or abrupt onset of symptoms
 Body aches and pains	Sometimes ?	Common	Common ?	No	No
 Diarrhea, nausea and vomiting	Sometimes?	Rare	Sometimes	No	No
 Chills	Sometimes	No	Sometimes	No	No
 Loss of taste or smell	! Sometimes	Rare	Rare	Rare	No

? Song X, JAMA Netw Open. 2020 Sep 1;3(9):e2020495



nasal polyps



Sources: Asthma and Allergy Foundation of America, World Health Organization, Centers for Disease Control and Prevention.  
edited 7/15/20 • aafa.org/covid19





# Take Home Messages



- Identification of a child with Covid-19 by mean of symptoms is a difficult task but we should try our best at least in a context of a clinical study.
- The most difficult task will be to distinguish the child with Covid-19 from the one with seasonal flu. 
- It should not be difficult to identify the allergic child or the child with asthma. 
- Allergic and asthmatic should continue and intensify their regular maintenance treatment to avoid symptoms which can erroneously inferred to Covid-19.
- Asthmatic children should be treated with MDI and spacer to avoid the risk of virus aero dispersion.





# Covid 19 :

## *the role of the pediatrician this fall and winter*



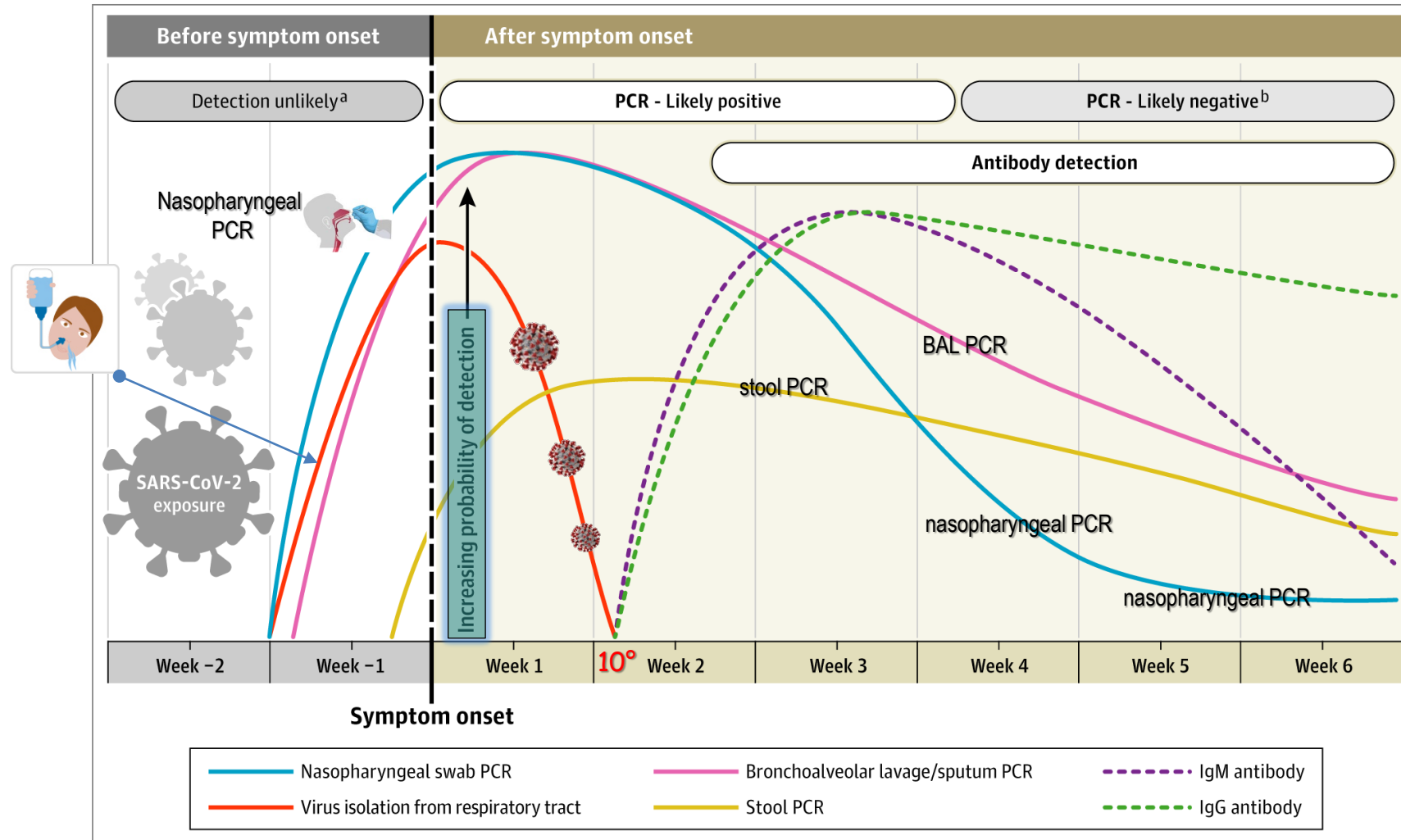
**Attilio Boner**  
**University of**  
**Verona, Italy**  
[attilio.boner@univr.it](mailto:attilio.boner@univr.it)

- ✓ Introduction: the second wave is coming
- ✓ Covid 19 no/yes by symptoms
- ✓ The case of the allergic child
- ✓ **Covid 19 testing**
- ✓ How to prepare the immune system
- ✓ The importance of nasal washing
- ✓ Waiting for a specific vaccine, do others !
- ✓ Summary & Conclusions

# Report from the American Society for Microbiology COVID-19 International Summit, 23 March 2020: Value of Diagnostic Testing for SARS-CoV-2/COVID-19.

*Patel R, mBio. 2020;11(2):e00722-20.*

## TEST 1. TESTS FOR VIRAL RNA





# Rethinking Covid-19 Test Sensitivity

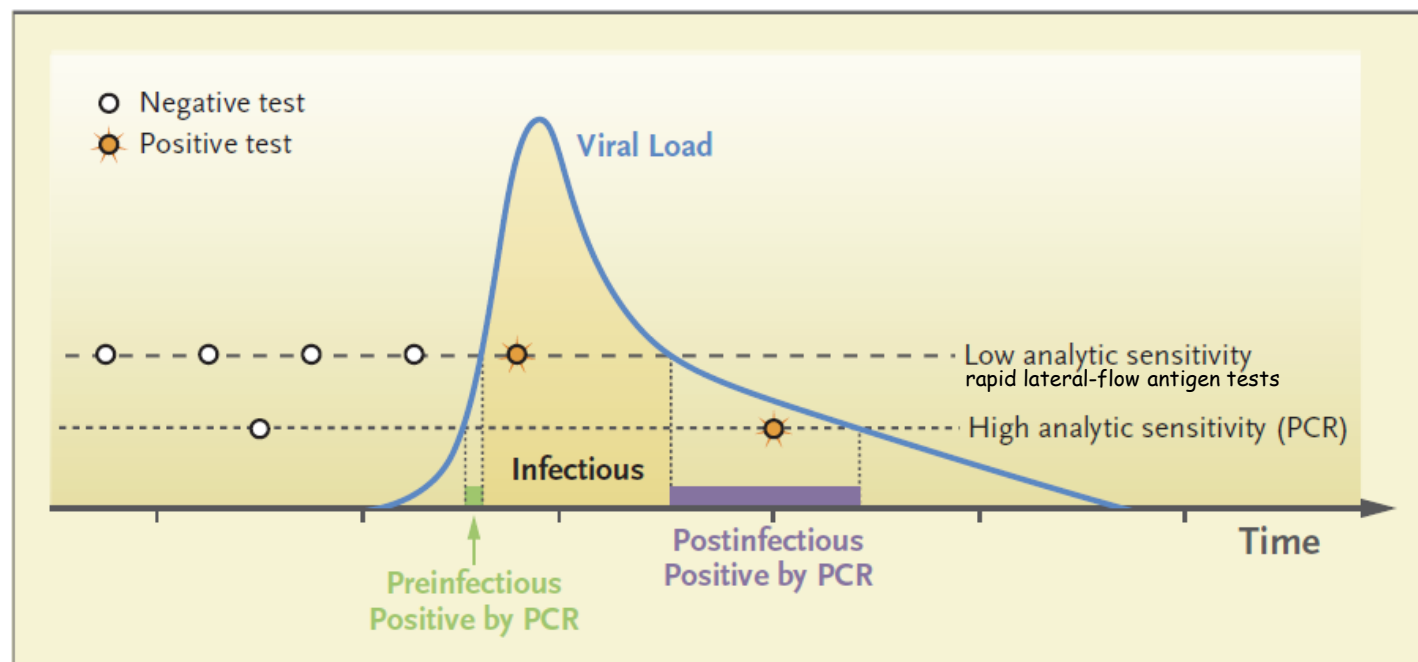
## - A Strategy for Containment.

*Mina MJ, N Engl J Med. 2020 Sep 30*

Dr. Michael Mina,  
an epidemiologist at  
the Harvard  
T.H. Chan School  
of Public Health,

High-Frequency Testing with Low Analytic Sensitivity  
versus Low-Frequency Testing with High Analytic Sensitivity.

- A person's infection trajectory (blue line) is shown in the context of 2 surveillance regimens (circles) with different analytic sensitivity.
- The low-analytic-sensitivity assay is administered frequently and the high-analytic-sensitivity assay infrequently.
- Both testing regimens detect the infection (orange circles), but only the high-frequency test detects it during the transmission window (shading), in spite of its lower analytic sensitivity, which makes it a more effective filter.
- The window during which polymerase chain reaction (PCR) detects infections before infectivity (green) is short, whereas the corresponding post infectious but PCR-detectable window (purple) is long.



# False Negative Tests for SARS-CoV-2 Infection - Challenges and Implications.

*Woloshin S, N Engl J Med. 2020;10.1056/NEJMp2015897.*

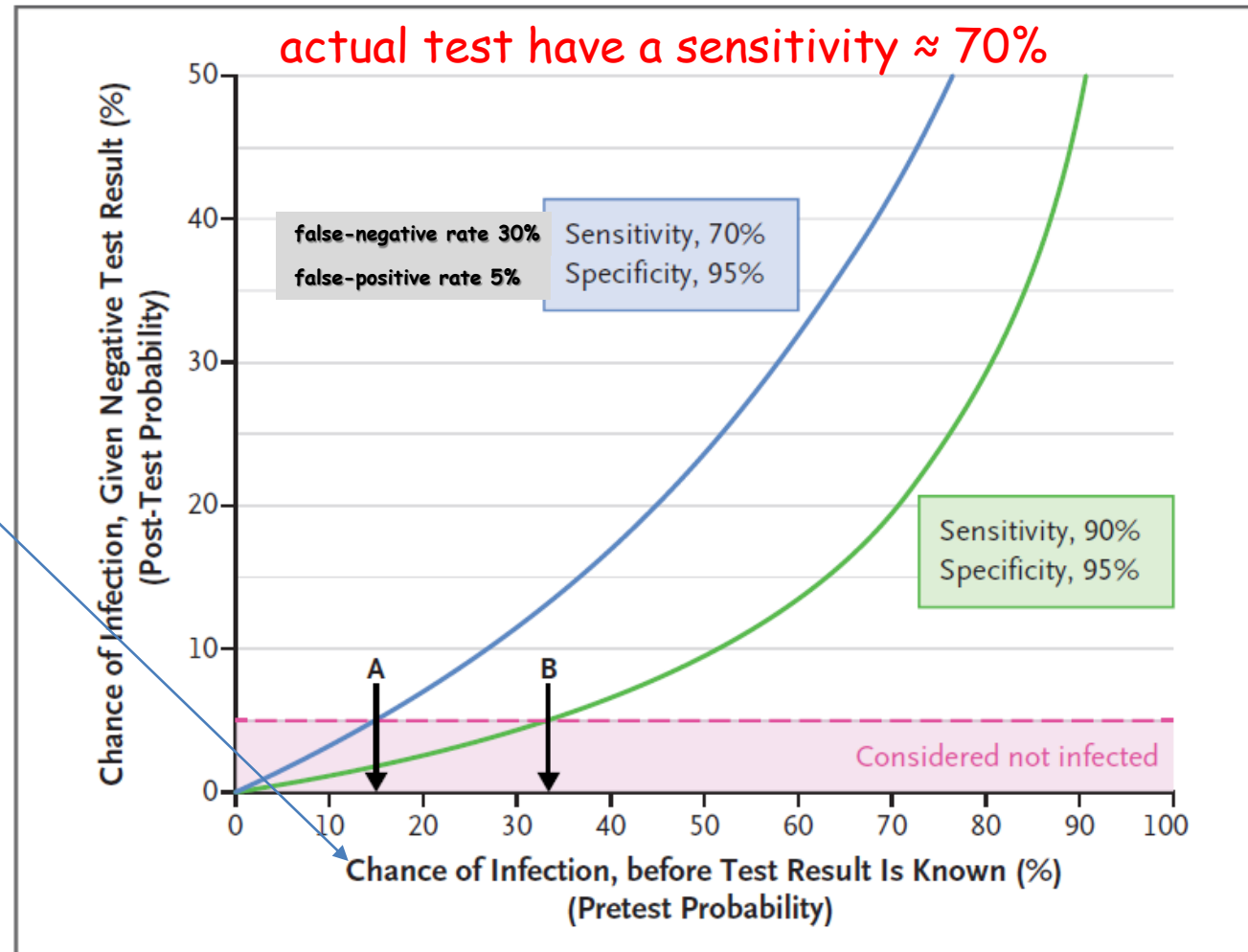
For a (-) test,  
there are 2 key inputs:

- i) pretest probability — an estimate, before testing, of the person's chance of being infected — and
- ii) test sensitivity.

Pretest probability depend on:

- local Covid-19 prevalence,
- SARS-CoV-2 exposure history, and
- symptoms.

Ideally, clinical sensitivity and specificity of each test would be measured in various clinically relevant real-life situations (e.g., varied specimen sources, timing, and illness severity).



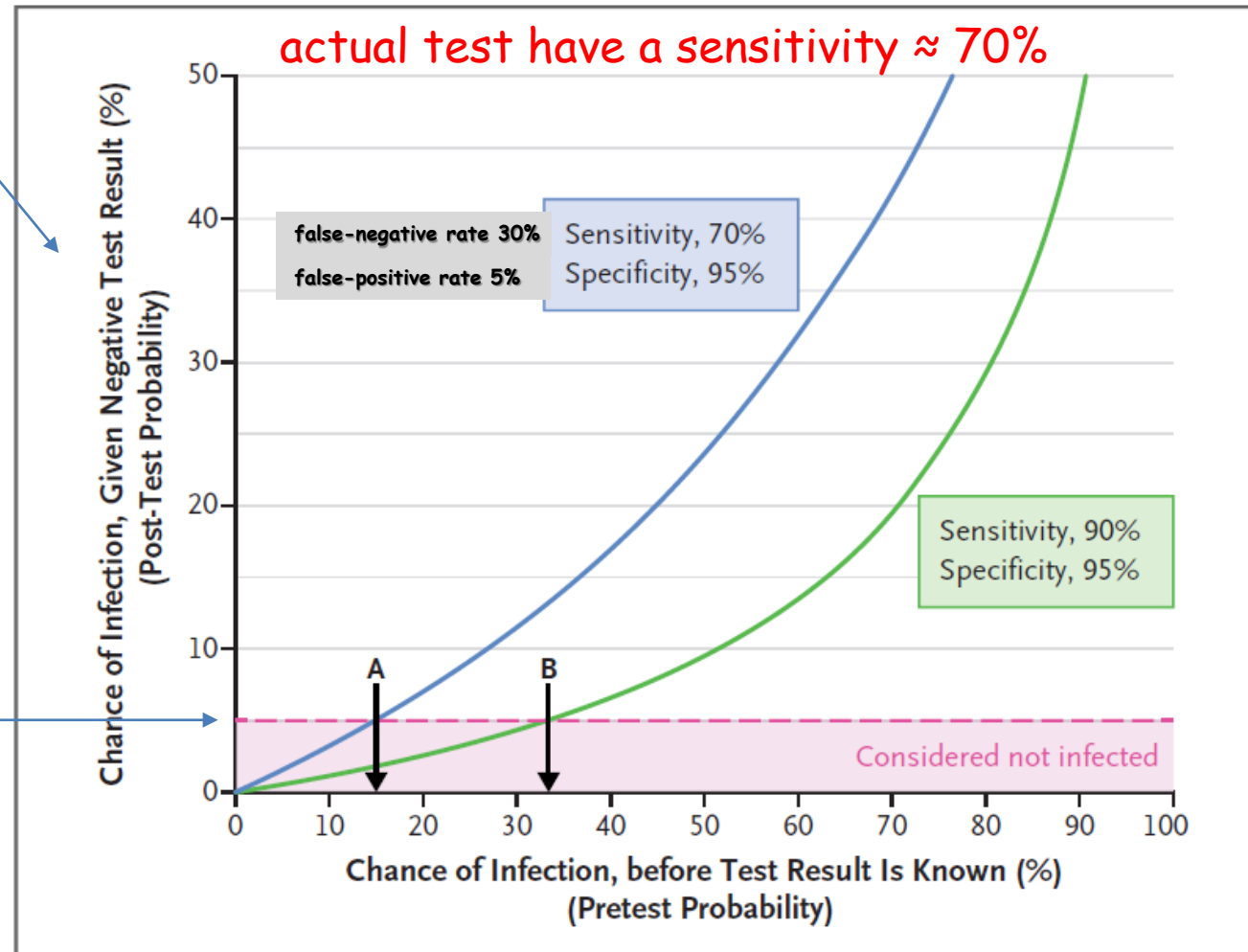
# False Negative Tests for SARS-CoV-2 Infection - Challenges and Implications.

*Woloshin S, N Engl J Med. 2020;10.1056/NEJMp2015897.*

The graph shows how the post-test probability of infection varies with the pretest probability for tests with low (70%) and high (95%) sensitivity.

The horizontal line indicates a probability threshold below which it would be reasonable to act as if the person were uninfected (e.g., allowing the person to visit an elderly grandmother or go to school).

Where this threshold should be set — here, 5% — is a value judgment and will vary with context (e.g., lower for people visiting a high-risk relative). The threshold highlights why very sensitive diagnostic tests are needed.

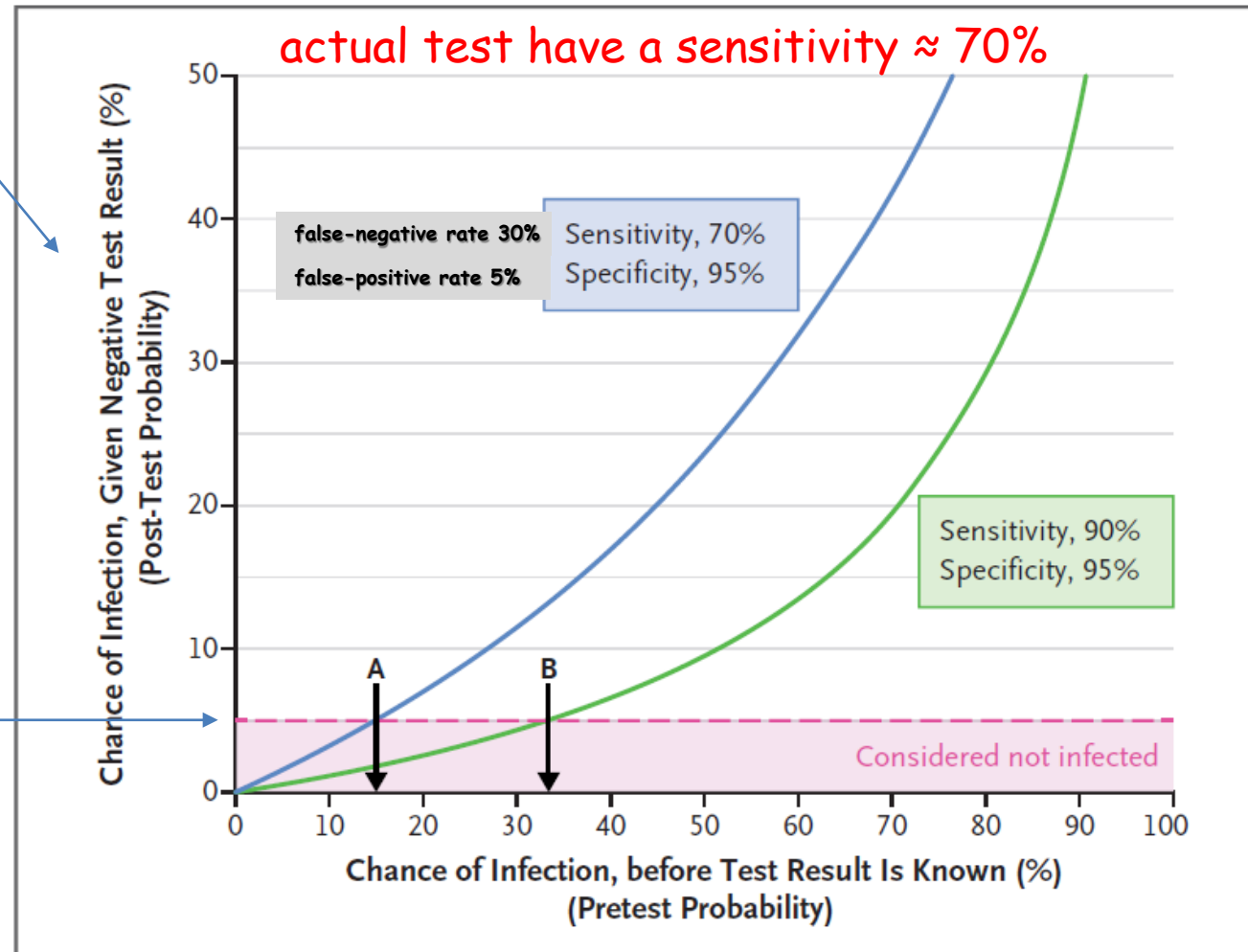


# False Negative Tests for SARS-CoV-2 Infection - Challenges and Implications.

*Woloshin S, N Engl J Med. 2020;10.1056/NEJMp2015897.*

The graph shows how the post-test probability of infection varies with the pretest probability for tests with low (70%) and high (95%) sensitivity.

*With a negative result on the low-sensitivity test (70%), the threshold of 5% is exceeded when the pretest probability exceeds **15%** (A), but with a high-sensitivity test, one can have a pretest probability of up to **33%** and still, assuming the 5% threshold, be considered safe to be in contact with others (B).*





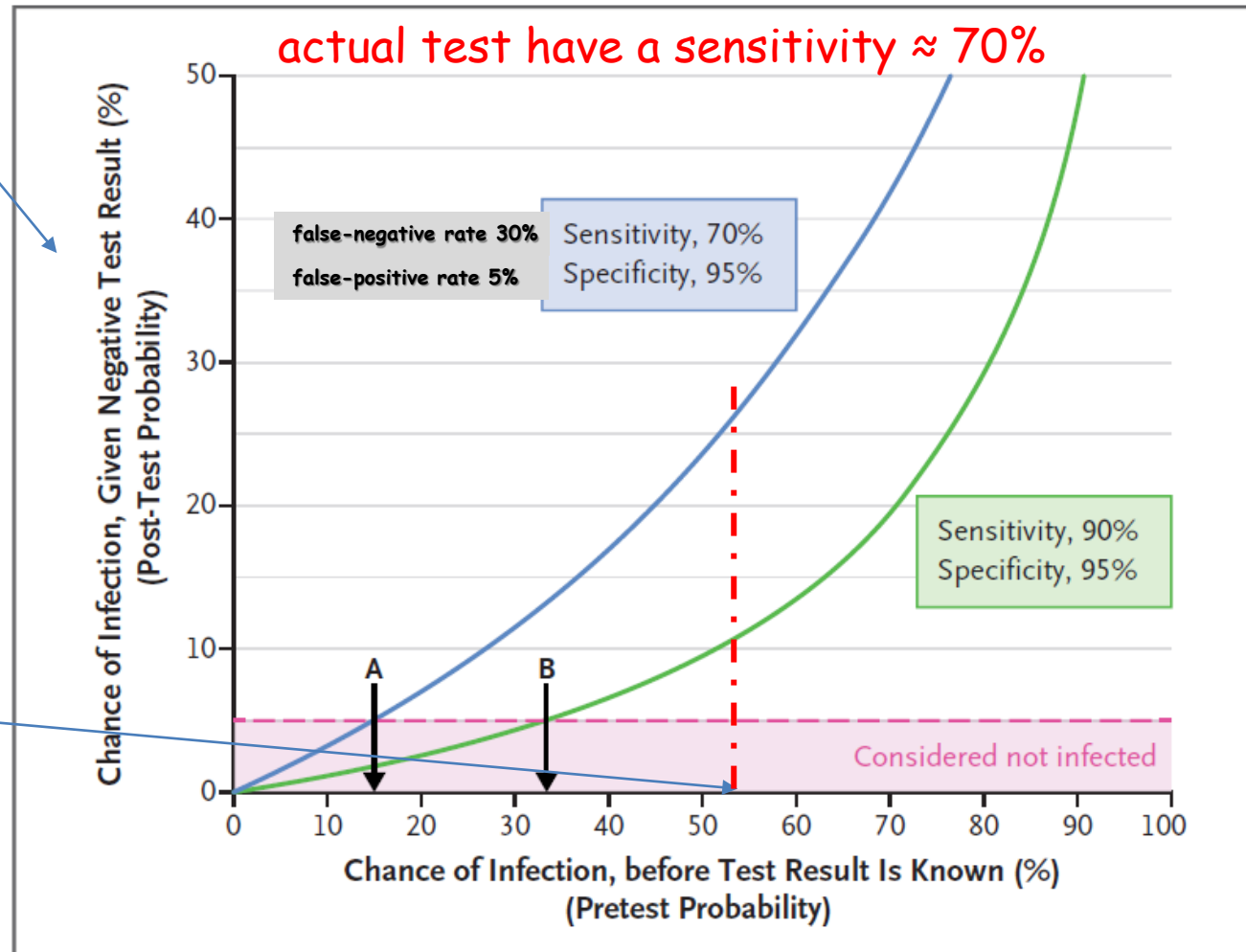
# False Negative Tests for SARS-CoV-2 Infection - Challenges and Implications.

*Woloshin S, N Engl J Med. 2020;10.1056/NEJMp2015897.*

The graph shows how the post-test probability of infection varies with the pretest probability for tests with low (70%) and high (95%) sensitivity.

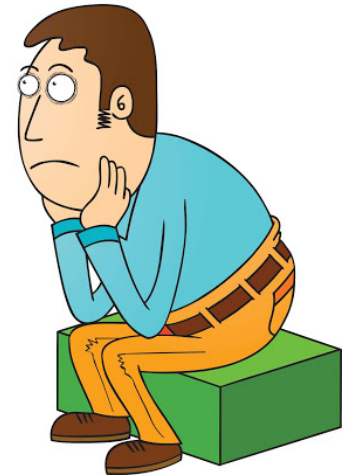
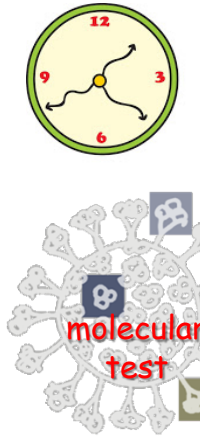
The graph also highlights why efforts to reduce pretest probability (e.g., by social distancing, possibly wearing masks) matter.

If the pretest probability gets too high (above 50%, for example), testing loses its value because negative results cannot lower the probability of infection enough to reach the 5% threshold.



# Why rapid test are necessary?

- A major problem with molecular tests is the **lag time** in receiving test results.
- a modeling study showed that:
  - same-day results can prevent 80% of new transmissions,
  - a **3-day testing delay** prevent 42% of new trasmission
  - a **7-day delay** stops only 5%.



*Kretzschmar ME, Impact of delays on effectiveness of contact tracing strategies for COVID-19: a modelling study. Lancet Public Health. 2020 Aug;5(8):e452-e459.*



# Take Home Messages



- To contain Covid 19 is essential:
  - Test people to uncover the virus
  - Track how and where the virus is spreading
  - Trace people who may be infected
- Different tests can be used in different contexts:
  - Hospitals
  - Office
  - Schools
  - Airports
- Rapid tests identifying virus antigen are less sensitive (>false negative) than RT-PCR-RNA
- Pretest probability of infection has to be considered when evaluating a negative test result